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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,249	11/03/2003	Toshimitsu Matsui	14014.0266U3	3780

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EXAMINER	
CHEU, CHANGHWA J	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/700,249	MATSUI ET AL.	
	Examiner	Art Unit	
	Jacob Cheu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/1/2004*.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election traverse of group VIII, claim 14 in the reply filed on 12/22/2005 is acknowledged.

2. New claims 15-21 are added and depend on claim 14.

3. Applicant argues that all the claims relate to a PDGF receptor, thus would not impose undue burden for search. Applicant's argument has been considered but not persuasive. All the groups direct to patentably distinct inventions with respect to patentably distinct product(s) and method of using. Because these inventions are distinct and have acquired separate status in the art as shown by their different classification, recognized divergent subject matter and because the search required for each invention is not substantially coextensive with the search required for the remaining invention, restriction for examination purposes as indicated is proper. Please note that the classifications in the restriction are illustrative only and do not represent all the classes and subclasses which must be searched for each invention; nor is the search limited to issued US patents, but rather includes published foreign patents and applications as well as literature search.

The Restriction Requirement is still deemed proper and is therefore made **FINAL.**

4. Currently claims 14-21 are under examination. Claims 1-13 are withdrawn from further consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter/Written Description

"fragment"

5. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant invention directs to a method of evaluating binding affinity of a test compound to α PDGFR or β PDGFR receptor. The method comprises contacting a sample containing the said receptors with an antibody specifically binds to α PDGFR or β PDGFR or a *fragment thereof* wherein the antibody is selectively from the group consisting of monoclonal antibody and polyclonal antibody (emphasis added).

Examiner notices that the "fragment" was originally recited referring to "antibody", not referring to either α PDGFR or β PDGFR (See claim 14). Examiner also points out the ambiguity of the "fragment thereof" with respect to which molecule, e.g. antibody or PDGFR, applicant refers to (See below 35 USC, 112 second paragraph rejection).

Assuming *arguendo*, this "fragment" refers to the α PDGFR or β PDGFR. The phrase is new matter lacking of support from the original filed specification.

Although "fragment" appears in numerous places from the specification, this term only refers to the cloning of the bulk piece of the PDGFR receptor. Nowhere the term "fragment" is used or implied for any fragment(s) within the PDGFR. For instance, section 0027-0028, the "fragments" refer to the antibodies, such as Fab or F(ab)' fragment. Figure 1, the fragments refer to hybridization of PDGFR with the antibody. Figure 6 and section 0045-47, 0050 and 0078, the "fragment" refers to the restriction site

for cloning, e.g. HindIII-PstI.). None of the data provide any information with respect to the "fragment" of PDGFR receptor.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. As discussed above, the skilled artisan cannot envision applicant had possessed the invention as recited for the "fragments" of PDGFR receptor. Therefore, the "fragment" is new matter.

Claim 20 and 21

6. Claim 21-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant recites in claim 21 and 21 that the antibody or fragment thereof is specific for a protein <u>*having*</u> the amino acid sequence of a human type α PDGFR and β PDGFR receptor protein, respectively (emphasis added).

The wording "having" denotes an open language, e.g. comprising, which could be interpreted the antibody or fragment thereof is specific for a protein that not only contains α PDGFR or β PDGFR, but also <u>*other*</u> amino acids (emphasis added). No support can be

found from the specification for such a protein. As discussed above, the skilled artisan cannot envision applicant had possessed the invention as recited antibody specific for amino acid sequence other than that of α PDGFR and β PDGFR pursuant to dictum of *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111.

Enablement

7. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth in *In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)*, enablement requires that the specification teach those skilled in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

Fragment

Regarding *fragments* of PDGFR, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. Particularly, the essential epitopes bound to the antibody. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and

in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis in Trend in Genetics Vol. 14, page 398; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133;)

Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, *without undue experimentation*, the essential positions in the protein which are critical for antibody binding and tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions.

Since the instant specification has not provided a precise disclosure of the fragments of the PDGFR recited in claim 14, one could not generate the antibodies recited in claim 14. Given that the antibodies required for the method of claim 14 cannot be generated, the method itself cannot be enabled.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 14, step (a)(i), line 1, "an antibody which specifically binds α PDGFR or β PDGFR or a fragment thereof" is vague and indefinite. It is not clear what "fragment thereof" modifies, whether this fragment refers to either the antibody or the PDGFR receptor. Applicant needs to clarify.

With respect to claim 15, it is not clear what "agonist" applicant refers to, e.g. to the antibody or PDGF receptor (alpha or beta).

With respect to claim 16, it is not clear what "antagonist" applicant refers to, e.g. to antibody or PDGF receptor (alpha or beta).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claim 14-19, and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Heldin et al. (applicant submitted on 3/1/2004, page 10, reference B7, EMBO 1988 Vol. 7, page 1387).

Heldin et al. teach a method of evaluating binding of different dimeric forms of PDGF, e.g. PDGF-AA, AB or BB, to human fibroblast having PDGFR receptors. Heldin et al. teach evaluating the binding affinity of the different dimers (test compounds) by contacting the fibroblast cells (containing PDGFR receptors) with test compounds, i.e.

PDGF-AA, AB, or BB dimers with an antibody which recognizes the β PDGFR on the fibroblast cells, and measuring the binding affinity with respect to each test PDGF dimers where the binding to the antibody is inversely proportional to the addition of each test dimers (See Figure 5).

With respect to claim 15-16, the results of the binding analysis indicate that PDGF dimers (AA, BB or AB) behave differently with respect to mitogenic effect as agonist and antagonist, respectively (See Figure 6).

With respect to claim 17-19, Heldin et al. use PDGF-AA, BB and AB isomers as the test compounds for the binding affinity analysis (See Methods and Materials and Figure 5-6).

With respect to claim 21, the antibody used in Heldin et al. study recognizing β PDGF receptor (See Abstract, and Method).

Conclusion

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-272-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner
Art Unit 1641

March 15, 2006

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
3/16/06